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The Importance of Neuromonitoring in Non Brain Injured Patients

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Introduction

The use of non-invasive neuromonitoring in patients without brain injury has increased over the past decades [1]. Most common clinical applications of noninvasive neuromonitoring in the non-neurological setting include the study of patients without primary brain injury but with a potential for neurological derangement. These clinical conditions include liver failure, post-cardiac arrest syndrome, severe respiratory failure with or without extracorporeal membrane oxygenation (ECMO) or extracorporeal carbon dioxide removal (ECCO2R), polytrauma, stroke, sepsis, pregnancy, pediatric population, and the surgical population in the periop-erative period [1]. In recent years, a growing literature has suggested the use of non-invasive techniques in this population, and these are becoming increasingly popular among general critical care physicians for daily and bedside patient management [1, 2]. The aim of this chapter is to provide anesthesiologists and intensiv-ists with an up-to-date view of the most frequent clinical conditions with potential for neurological complications in patients without brain injury, and to describe the role of non-invasive multimodal neuromonitoring in the early identification and management of these complex scenarios.

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Basics of Neuromonitoring in Anesthesia and Critical Care

In this paragraph, we will introduce the most commonly used non-invasive neuro-monitoring tools in anesthesia and in the critical care settings. However, a detailed description of each neuromonitoring system is beyond the aim of the present manuscript, and the reader should refer to the dedicated literature.

Table 1 presents the methodology, strengths, and limitations of the main neuromonitoring techniques (electroencephalography [EEG], processed EEG [pEEG], somatosensory evoked potentials [SSEPs] and motor-sensory potentials [MEPs], transcranial Doppler [TCD], optic nerve sheath diameter [ONSD], pupillometry, and near-infrared spectroscopy [NIRS]).

Clinical Applications

Neuromonitoring in the Operating Room

Intraoperative and postoperative neurological complications, such as delirium, postoperative cognitive decline, stroke, spinal cord ischemia, and postoperative visual loss, are frequently underestimated [2]. These complications have the potential to increase mortality and morbidity and should therefore be promptly identified and prevented [2]. Some types of surgery are more susceptible than others to cerebral complications. In major vascular surgery, registries have reported an intra/postoperative stroke rate of 7% after carotid stenting and of 3.2% after endarterectomy [3]. During aortic procedures,

Table 1 Basic functioning of different neuromonitoring devices

Type	Methodology	Strengths (S) and limitations (L)	Action of medications
EEG	EEG gives information about cortical activity Global information Scalp electrodes	S: Global information of cerebral activity L: EEG trace needs experienced operators for interpretation	Ketamine increases the activity of excitatory neurons and high frequency oscillations Nitrous oxide increases the amplitude of high frequency activity Dexmedetomidine causes slow oscillations with deeper sedation but easily awakened patient Propofol increases theta, alpha, spindle beta power, slow waves and delta activity
pEEG	Translation between analogic signal of EEG to digital (numeric). Awake status = 100; general anesthesia = 40–60; suppressed EEG = 0 Regional information Adhesive pads DSA is a colored trace obtained from EEG frequencies and transformed into decibels of bi-hemispheric activity that can change from red (more frequent) to blue (rare)	S: Bedside application S: Easy interpretation S: Availability L: Muscle artifact L: Translation between analogic signal of EEG to digital L: Delay between event and measure L: Cerebral activity in limited area (frontal) L: Several noisy elements can interfere with the signal L: Effects of medications L: Validation in non-older adults	Ketamine increases the activity of excitatory neurons and high frequency oscillations Nitrous oxide increases the amplitude of high frequency activity Dexmedetomidine causes slow oscillations with deeper sedation but easily awakened patient Propofol induces slow waves, until suppressed pEEG with increases in dosage Sevoflurane effects on BIS are unclear
Type	Methodology	Strengths (S) and limitations (L)	Action of medications
SSEPs	SSEPs measured by stimulating a peripheral sensory nerve and recording the signal transmitted to the sensory cortex Bedside application	S: Bedside application S: Availability L: Interference with electric devices L: Interpretation by expert	Ketamine increases cortical SSEP amplitude Dexmedetomidine affects amplitude minimally Propofol has minimal effects on SSEPs. Sevoflurane affects SSEPs in a dose-dependent way Barbiturates increase latency and decrease amplitude of SSEPs Benzodiazepines reduce amplitude and increase latency Opioids do not significantly affect SSEPs, but remifentanil prolongs SSEP latency
MEPs	MEPs measured by transcranial stimulation of the cortex and recording the signal at the spinal cord level, peripheral motor nerves, or the muscles	S: Bedside application S: Availability L: Interference with electric devices L: Interpretation by expert equipment	Ketamine increases amplitude at increased frequency of MEPs Dexmedetomidine causes a decrease in MEP amplitude Propofol has excitatory effects on MEPs Sevoflurane has a depressant effect on MEPs Benzodiazepines attenuate MEPs

Table 1 (continued)

Type	Methodology	Strengths (S) and limitations (L)	Action of medications
TCD	Investigation of local blood flow and velocities in the circle of Willis 2 mHz probe placed in acoustic windows (i.e., transtemporal) Measure of nICP and eCPP Cerebral autoregulation Critical closing pressure Diastolic closing margin Midline shift Emboli, obstruction, stenosis	S: Bedside application S: Availability L: Need for experienced operators L: Availability of windows	Ketamine may affect cerebral hemodynamics Propofol decreases the tone of the venous capacitance vessels and decreases cerebral metabolism Remifentanil reduces cerebral blood flow velocity despite constant perfusion pressure Thiopental decreases CBF velocities Benzodiazepines decrease CBF velocity
ONSD	Measure of nICP and eCPP	S: Bedside application S: Easy interpretation S: Availability	ONSD is larger with propofol in comparison to sevoflurane
Pupillometry	Pupillometry measures the diameter of	S: Bedside application	Remifentanil determines miosis and reduces
	the pupils and the pupillary light reflex	S: Easy interpretation	PLR
	NPi is an algorithm using parameters to	S: Availability	Propofol determines miosis and reduces CV
	determine pupillary light response, with a	L: Agitated or confused patients can be	Barbiturate titrated to burst suppression
	scale 0–5, < 3 is abnormal	difficult to evaluate	reduces CV
	Maximum and minimum pupil diameter	L: Patients with scleral edema, periorbital	Droperidol causes miosis and reduces PDR
	(mm) refers to diameter at rest and peak	edema, intraocular lens replacement prior	Metoclopramide causes miosis and reduces
	constriction Latency is the time (seconds) delay between light stimulus and pupillary constriction	ocular surgical procedures can limit assessment with pupillometry L: Ambient light can influence the measure L: Expensive	PDR
	CV is the distance (mm) of constriction divided by duration (seconds) of constriction		
	Dilation velocity is the distance (mm) of re-dilation divided by duration (seconds) of re-dilation		
ype	Methodology	Strengths (S) and limitations (L)	Action of medications
NIRS	NIRS measures cerebral oxygen	S: Bedside application	Propofol and dexmedetomidine equally
	saturation by using a near-infrared light	S: Easy interpretation	preserve cerebral oxygenation and do not
	passing through adhesive pads and	S: Availability	affect neurological outcome
	tissues. The light is therefore adsorbed by	L: Regional evaluation of cerebral oximetry	Cerebral oxygenation may be better preserved
	oxyhemoglobin and deoxyhemoglobin, thus obtaining a value reflecting the local	that may not reflect global changes in hemodynamics	with sevoflurane than propofol Midazolam and morphine may alter cerebral
	amount of oxygen within the frontal region A decrease of 20% from baseline can be associated to the reduction of CBF, hypoperfusion and neurologic symptoms Regional measure	L: Bias with skin color and gender L: Variations due to systemic extracranial perfusion L: Elimination of oxygen degradation products in patients with liver diseases that can alter the absorption of light	oxygenation and hemodynamics
	Adhesive pads		

Table 1 (continued)

Type	Methodology	Strengths (S) and limitations (L)	Action of medications
	Various devices are available with different algorithms and components, including Masimo (Masimo Corp., Irvine, CA), INVOS (Medtronic, Minneapolis, USA)		

EEG electroencephalogram, *pEEG* processed EEG, *BIS* Bispectral index, *DSA* density spectral array, *ONSD* optic nerve sheath diameter, *CBF* cerebral blood flow, *SSEPs* somatosensory evoked potentials, *MEPs* motor sensory evoked potentials, *TCD* transcranial Doppler, *nICP* non-invasive intracranial pressure, *eCPP* estimated cerebral perfusion pressure, *CV* constriction velocity, *NPi* Neurological Pupil index, *PLR* pupillary light reflex, *PRD* pupillary reflex dilation

the T4-T8 segment is particularly susceptible to reduced blood perfusion, because of the variable location of the radiculomedullary arteries and of the artery of Adamkiewicz; this may influence pathological processes and the metabolic state of the tissue during aortic surgery, thus causing paralysis in the worst cases [3]. During thoracic aorta surgery, following the circulatory arrest with consequent transient ischemia, an early phase of parenchymal hypoperfusion is present, with consequent systemic inflammation and possible reperfusion injury. This results in a potential for severe temporary or permanent neurologic dysfunction including possible ischemic stroke, prolonged obtundation, disorientation, Parkinson-like movements, and loss of cognitive function [3, 4].

Similarly, in cardiac surgery, neuronal and vascular damage, inflammation, and embolism may result in inadequate oxygen delivery to the brain and altered cerebral autoregulation, predisposing to neurological complications [4]. Indeed, neurocognitive dysfunction, including postoperative delirium, effects up to 50% of patients after cardiac surgery, with stroke affecting 2%, and postoperative neurocognitive dysfunction up to 42% [4].

In addition, neurological complications can also occur following non-high-risk surgery. Some trials have revealed that use of adequate neuromonitoring during anesthesia can prevent or limit the occurrence of adverse effects [2]. Standard monitoring during anesthesia includes mainly hemodynamic and respiratory parameters among essential minimum monitoring data [5]. However, the primary targets of anesthetics and analgesics are the central and peripheral nervous systems [2]. It seems logical to assume that this ironic clinical gap in standards of monitoring during anesthesia deserves further revision, or at least should be individualized and implemented in case of predisposing comorbidities, perioperative events, and high-risk procedures [2].

In this section, we describe the most common clinical scenarios for potential of brain injury in the operating room and the utility of each neuromonitoring system in the early identification of such devasting complications. Table 2 resumes the most common clinical applications of neuromonitoring in the operating room.

Electroencephalography

pEEG monitoring was primarily introduced into the operating room to reduce the risk of awareness during surgery, to optimize anesthetic titration, and to individualize the depth of anesthesia [6]. The main raw traces identified by pEEG are shown in Fig. 1, panel A, while an example of a density spectral array (DSA) trace is presented in Fig. 1, panel B. In 2017, the European Society of Anesthesiology (ESA) produced a consensus suggesting that all patients undergoing surgery should have anesthesia depth monitored [7]. EEG responses to anesthesia depend on the interaction between surgical stimulus, sedatives, and anesthetic plane. The phase of induction of anesthesia is characterized by an increase in beta activity (13–30 Hz), followed by the maintenance phase which is characterized by an increase of alpha (8–12 Hz) and delta (0–4 Hz) activities, while during the emergence phase, a reverse order of frequencies appears. A numeric index between 40–60, which is the result of the integration of the raw signals, is recommended to avoid awareness and excessive sedation [2]. The use of pEEG devices has been validated to reduce awareness in patients receiving volatile anesthetics with a minimum alveolar concentration (MAC) value < 0.7, and during total intravenous anesthesia [2]. Moreover, pEEG may reduce drug consumption, thus reducing the incidence of postoperative nausea and vomiting and facilitating extubation and earlier discharge [2]. The intraoperative use of pEEG has been shown to reduce the incidence of delirium, cognitive dysfunction, and ischemic stroke in the postoperative period [2].

In major vascular surgery settings, the presence of beta bands, a decrease of more than 50% of background activity, a reduction in amplitude of 60%, an increase in delta and slow wave activities, or a complete loss of signal is highly suggestive for ischemic complications [8]. Of note, during carotid endarterectomy, changes in cerebral blood flow (CBF) frequently reflect on the EEG within 20–30 s after clamping [3]. When using pEEG, a reduction in bispectral index (BIS) value has also been correlated to ischemia and neurological deficit [9].

In cardiac surgery, long-term EEG burst suppression has been associated with postoperative neurocognitive dysfunction and delirium [4], while decreased alpha and beta waves can be indicative of a CBF < 22 ml/100 g brain tissue/ minute, and further reduction to 7-to-15 ml/100 g/min can result in an isoelec-tric EEG [4]. However, a recent large randomized controlled trial (RCT) did not support the use of EEG-guided anesthetic administration for the prevention of postoperative delirium in major surgery [10]. EEG or pEEG monitoring might also be useful to detect and avoid periods of burst suppression, which have been associated with postoperative delirium. However, evidence is still lacking on this topic [4].

Evoked Potentials

Evoked potentials are restricted to specific procedures, since their use often requires dedicated equipment and training. During carotid endarterectomy, hypoperfusion of the middle cerebral and anterior cerebral arteries could be detected by abnormalities in the SSEP signal at the median and tibial nerves [3]. Information from evoked

Table 2 Clinical application of neuromonitoring in the operating room

Type of surgery/ procedure	Neurological complications	Neuromonitoring	Evidence
Major vascular surgery	Stroke, delirium, cognitive decline, paralysis	EEG or pEEG	Beta bands, slow background, reduction of amplitude on EEG, reduction of BIS on pEEG are signs of ischemia (carotid surgery)
		Evoked potentials	Abnormalities in the SSEPs of median and tibial nerves if hypoperfusion (carotid surgery). MEPs correlate with NIRS
		TCD	TCD can allow detection of stenosis, turbulence, and emboli (carotid surgery)
		NIRS	Cerebral rSO2 < 70% is indicative of possible hypoperfusion (carotid surgery), lumbar rSO2 < 75% for 15 min can cause spinal cord injury (aortic repair)
Cardiac surgery	Delirium, cognitive dysfunction, stroke	EEG or pEGG	Long-term EEG burst suppression is associated with cognitive dysfunction and delirium. Decrease in alpha and beta waves is indicative of tissue hypoperfusion
		Evoked potentials	Help in the detection of ischemia, not specific
		TCD	TCD can detect changes in CBF, microemboli, flow asymmetries
		NIRS	An rSO2 value which falls by 10–20% or < 50% is associated with postoperative complications. The threshold of rSO2 > 80% prevents complications
Abdominal surgery	Neurological deterioration, intracranial hypertension	TCD	TCD can allow non-invasive calculation of ICP, identification of changes in CBF due to high ICP or carbon-dioxide vasodilatation
Orthopedic surgery	Cerebral deoxygenation	NIRS	Cerebral rSO2 monitoring can prevent cerebral deoxygenation and neurological complications

EEG electroencephalogram, *pEEG* processed EEG, *TCD* transcranial Doppler; *NIRS* near infrared spectroscopy, *BIS* Bispectral index, *rSO2* regional saturation of oxygen, *MEPs* motor evoked potentials, *SSEPs* sensory evoked potentials, *CBF* cerebral blood flow, *ICP* intracranial pressure

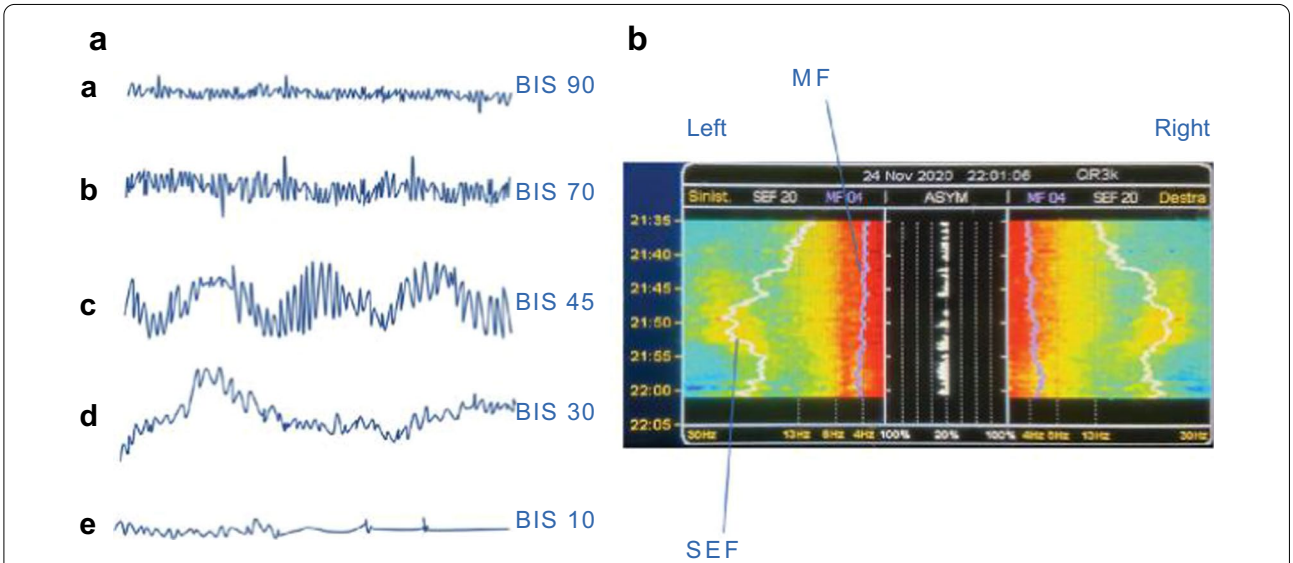

Fig. 1 Processed electroencephalography (pEEG). The main raw traces identified by pEEG are shown in Panel A: (**a**) small amplitude, fast frequency wave (patient awake), (**b**) moderate sedation, (**c**) large amplitude, slow frequency wave (general anesthesia), (**d**) slow oscillations (deep anesthesia), (**e**) isoelectric trace and burst suppression. The density spectral array (DSA), a colored trace obtained from EEG and transformed into decibels of bi-hemispheric activity that can change from red (highest powers) to blue (lowest powers), is shown in Panel B. The white line in the DSA represents the spectral edge frequency (SEF) (in Hertz); 95% of the power of the brain resides below that line. The purple line in the DSA in the median frequency (MF). *BIS* bispectral index

potentials has the advantage of being objective and providing quantitative information on neurological complications, but during surgery the signal may be modified by general anesthetics, and in particular volatile agents. SSEPs may also have high false-positive rates (40–67%) and a moderate false-negative (13%) rate, and a delayed response for spinal cord ischemia. Indeed, during aortic surgery, the blood flow is more often compromised in the anterior motor tract than in the sensory dorsal column, and the limited ability of evoked potentials to detect altered motor function during ischemia in case of isolated spinal injury becomes even more worrisome [11].

Transcranial Doppler

TCD flows of the main intracranial arteries are shown in Fig. 2. There are still no clear indications for TCD in the perioperative setting, but some authors have suggested its use during liver transplant for the detection of cerebral complications and in particular brain edema [12]. During pneumoperitoneum and the Trendelenburg position, TCD can also be considered for the detection of episodes of high intracra-nial pressure (ICP) [13] following increases in carbon dioxide (CO2) that can result in cerebral vasodilatation [14].

The beach chair position is a technique used for shoulder surgery, which has shown to put the patient at risk of neurological complications as it may decrease cerebral perfusion due to blood pressure fall [15]. Moreover, major orthopedic surgery is a discipline at high risk of microembolic complications and TCD may help in the early diagnosis of embolic stroke in the perioperative period [16].

TCD in major vascular surgery can detect isolated arterial stenosis, which results in focal velocity increase and turbulence, inadequate collateral flow after proximal carotid cross-clamping by detecting compromised flow, and high-intensity signals at the Doppler spectral waveforms that can be indicative of emboli [17].

Finally, TCD is frequently used in cardiac surgery to detect changes in flow velocities and flow asymmetries and can be a valid option to assess anterograde cerebral perfusion during aortic arch surgery and for the detection of high-intensity signals related to microemboli [18, 19].

Near-Infrared Spectroscopy

NIRS can provide important information on changes in cerebral oxygenation during the perioperative period, but NIRS signals can be modified by anesthetics and sedatives. In orthopedic surgery, NIRS has been used together with TCD during the beach chair position to prevent cerebral deoxygenation with good effect [16], but its use is

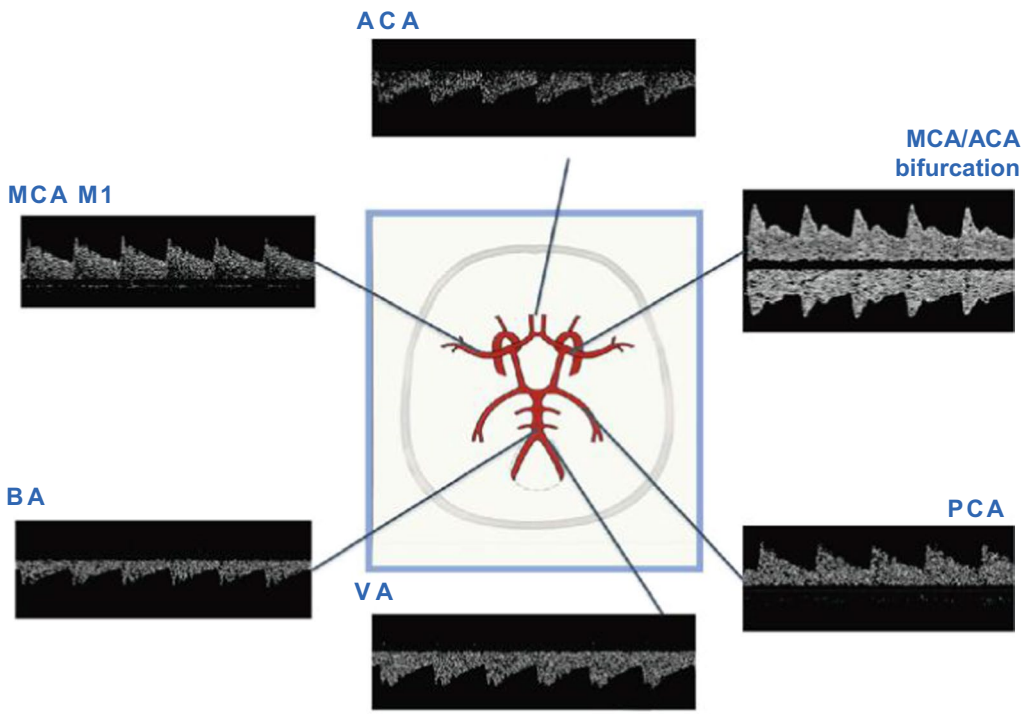

Fig. 2 Transcranial Doppler monitoring. The circle of Willis is represented in red with specific transcranial color Doppler sonographic images for each intracranial artery. *MCA* mean cerebral artery, *PCA* posterior cerebral artery, *ACA* anterior cerebral artery, *VA* vertebral artery, *BA* basi-lar artery

specifically recommended in major vascular and cardiac surgery [4, 20].

In carotid surgery, a regional cerebral oxygen saturation (rSO2) of < 70% (50 to 75%) has been suggested as a possible indicator of hypoperfusion, and in patients undergoing aortic repair, a lumbar rSO2 of < 75% for 15 min predicted the development of spinal cord injury [4, 20]. The sensitivity of NIRS in detecting cerebral ischemia is 60–100% with good specificity (94–98%) [20], although neurological monitoring and awake anesthesia remain the gold standard [21].

NIRS has also been recommended in cardiac surgery, both in the preoperative and intraoperative periods, to detect patients at higher risk of neurological complications and to identify episodes of acute cerebral hypoperfusion, which are common in these settings [22]. Cerebral oximetry should be cautiously interpreted, considering the baseline values and its trend, as well as preoperative patient status [22]. A recent meta-analysis assessing preoperative rSO2 values in cardiac surgery found a reference range of between 51 and 82%, with a mean baseline value of 66% [23]. According to the literature, intervention is needed when the rSO2 values decrease by 10–20% from baseline or below the absolute value of 50%; moreover, the time spent with rSO2 < 50% is significantly associated with the occurrence of postoperative delirium during coronary artery bypass graft surgery [23].

Figure 3 shows an example of cerebral oximetry using the Masimo (Masimo Corp., Irvine, CA) device.

Neuromonitoring in the Emergency Department and Intensive Care Unit

Neuromonitoring in the emergency department (ED) and ICU might be a valuable complement to clinical diagnosis and diagnostic images in patients without primary brain injury who are at risk of cerebral hemodynamic impairment [24]. Neurological impairment is common in patients admitted to the ED and ICU with sepsis, metabolic, renal, or hepatic diseases, and intoxication as these conditions can cause encephalopathy, cognitive decline, and delirium [24]. Additionally, a large potential for brain injury should be considered in patients with polytrauma, in the context of focused assessment with sonography in trauma (FAST) [25, 26].

Despite the diagnostic and prognostic potentiality of non-invasive multimodal neuromonitoring in the ED, use of these techniques is still limited in these settings, and they are currently more frequently adopted in post-emergency settings after ICU admission. Table 3 resumes

Fig. 3 Near infrared spectroscopy. This figure represents two possible traces, one with normal values and the other with abrupt decrease in regional oxygen saturation (rSO2) values. *ΔO2Hbi* index associated with variation of the oxygenated component of the hemoglobin in the total calculation of rSO2 (arterial component of rSO2), *ΔHHbi* an index associated with variation of the deoxygenated component of hemoglobin within the total calculation of rSO2 (venous component of rSO2), *ΔcHbi* is the sum of ΔHHbi + ΔO2Hbi. SpO2—rSO2 is the difference between the value of peripheral saturation of oxygen (SpO2) and rSO2

Table 3 Clinical application of neuromonitoring in the emergency department and intensive care unit

Setting	Neurological complications	Neuromonitoring	Evidence
Cardiac arrest	Neurological outcome	EEG or pEEG	Prognostication after cardiac arrest
		Evoked potentials	Prognostication after cardiac arrest (SSEPs) after 48–72 h
		TCD	Detection of CBF abnormalities and intracranial hypertension
		Pupillometry	Prognostication after cardiac arrest
Brain death	Diagnosis	EEG or pEGG	Electrocerebral silence
		TCD	Detection of flow inversion, intracranial hypertension. Ancillary test
		Pupillometry	No response
ECMO	Neurological outcome	EEG or pEGG	Prognostication in patients receiving ECMO
		TCD	CBF alterations, stroke
		NIRS	Association with neurological injury
ARDS and COVID-19 ARDS	Neurological complications, delirium	EEG or pEGG	Typical EEG includes abnormal background, epileptiform discharges in only 20%
		TCD	Pulmonary shunt, microemboli, CBF alterations, cerebral autoregulation
		NIRS	To detect brain deoxygenation, and responses to hemodynamic and respiratory maneuvers
		Pupillometry	Inconclusive evidence
Liver diseases	Encephalopathy	TCD	High resistances on TCD, CBF alterations
		NIRS	Association with outcome
		Pupillometry	Pupillary abnormalities are associated with neurological complications
Kidney disease	Encephalopathy	TCD	CBF alterations
		NIRS	Association with outcome
Sepsis	Encephalopathy	TCD	High resistances on TCD, altered CBF, high PI. Association between PI and delirium
		NIRS	Association with outcome
		Pupillometry	Pupillary abnormalities are associated with neurological complications

EEG electroencephalogram, *pEEG* processed EEG, *TCD* transcranial Doppler, *NIRS* near infrared spectroscopy, *BIS* Bispectral index, *rSO2* regional saturation of oxygen, *SSEPs* sensory evoked potentials, *CBF* cerebral blood flow, *ICP* intracranial pressure, *PI* pulsatility index, *ARDS* acute respiratory distress syndrome, *COVID-19* coronavirus disease 2019, *ECMO* extracorporeal membrane oxygenation

some of the most common clinical applications of neuromonitoring in the ED and ICU.

Electroencephalography

EEG is mainly used in the ED for the early diagnosis of first-time seizures that are often caused by non-primary brain injury, such as with systemic fever and metabolic disturbances [27]. The utility of pEEG in the ED has been poorly investigated, but it may potentially be used in patients who need sedation for various reasons, to assess the occurrence of burst suppression, to help in the induction of anesthesia, and to monitor brain activity for any causes [9, 28, 29].

In the ICU setting, in addition to the detection of seizures or status epilepticus, one of the main applications of EEG is in the assessment of patient prognosis [30], in particular with the detection of a suppressed EEG in case of vegetative state and electrocerebral silence in brain death [31]. This is particularly useful in cardiac arrest patients [31].

In patients receiving ECMO, EEG has shown to be useful in the identification of patients at risk for neurological complications and to predict poor outcome, by the identification of specific patterns, such as suppression [32] and absence of EEG reactivity [33]. Abnormal background abnormalities have also been demonstrated to be common EEG features of patients with coronavirus disease 2019 (COVID-19), with an incidence of 96%, while epileptiform discharges were present in 20% of patients [34].

Evoked Potentials

Evoked potentials are frequently used for neuroprognostication in specific diseases (e.g., traumatic brain injury [TBI], cardiac arrest) as part of multimodality algorithms that include clinical examination, electrophysiologic testing, imaging, and laboratory markers (e.g.,

serum enolase) [31]. Following cardiac arrest, SSEPs are still considered a cornerstone of prognostic algorithms, especially when delayed 48–72 after cardiac arrest [31]. Typical patterns of SSEPs in the median nerve following cardiac arrest include: bilaterally negative N20, which is indicative of death or vegetative state and poor prognosis; presence of N20 potentials and absent mismatch negativity, which is diagnostic of indeterminate prognosis; and presence of N20 with mismatch negativity, which represents a 95% chance of recovery with good neurological function [31].

Transcranial Doppler

TCD has considerable diagnostic potential in the ED and the ICU. Hepatic encephalopathy is a complication which occurs in up to 70% of patients with liver cirrhosis, and that manifests with psychomotor, attentive, and executive alterations [35].

Higher vascular resistances and pulsatility index in the middle and posterior cerebral arteries of cirrhotic patients have been reported in comparison to controls, with 74% accuracy of the middle cerebral artery resistive index for discriminating the presence of hepatic encephalopathy [35].

Alterations in CBF have also been found in patients with uremia and chronic kidney disease, typically with a decrease in CBF observed after hemodialysis [36].

Sepsis-associated encephalopathy is considered as an independent risk factor for mortality [37] that is characterized by a decrease in the density of cerebral microvessels that can alter cerebrovascular resistances, with potential for inadequate oxygen supply and cerebral dysfunction. On TCD, the pulsatility index was higher in septic patients than in controls [38], and high pulsatility index values on the first day of sepsis diagnosis were associated with a positive CAM-ICU delirium assessment [39]. TCD after cardiac arrest has been extensively studied, and includes four different features: pulsatility index < 0.6 (very low resistance), associated with possible hyperemia, vasospasm or stenosis; pulsatility index 1.2–1.6 (high resistance) with possible microangiopathy or mild intracranial hypertension; pulsatility index 1.7–1.9 (very high resistance) with severe intracranial hypertension; and pulsatility index ≥ 2 with cerebral hypoperfusion. In patients who remain comatose > 20 min after return of spontaneous circulation the main pattern described is a high pulsatility index [40].

In patients with polytrauma admitted to the ED at risk for intracranial hypertension or with contraindications to invasive ICP placement, TCD and ONSD can be a valid option for the assessment of high ICP and for excluding extracranial hypertension [25, 26].

In mechanically ventilated patients with acute respiratory distress syndrome (ARDS) (including COVID-19 ARDS), TCD has been extensively used and has the potential to indicate the effect of mechanical ventilation strategies on cerebral function, to detect secondary brain dysfunction, and to assess cerebral autoregulation during hemodynamic and respiratory rescue maneuvers [41–43].

Near Infrared Spectroscopy

The use of NIRS is gaining increasing interest in the ED and ICU settings to detect microcirculatory changes in patients with septic or metabolic alterations. Although the majority of studies have been conducted in the ICU, some studies in the ED have concluded that NIRS may correlate with severity of illness, especially after cardiac arrest, with variable association between rSO2 values and outcome [44, 45]. NIRS has been also used for the evaluation of cerebral complications and out come in sepsis, with a rSO2 cut-off of 75% as predictor of neurological sequelae [46]. Similarly, an increase in rSO2 during hospitalization, and lower tissue oxygen extraction rates detected using NIRS, have been shown to be associated with improved survival in polytrauma patients [47].

Finally, in mechanically ventilated patients with ARDS (and COVID-19 ARDS), NIRS has been shown to be useful in assessment of the effect of hemodynamic and respiratory maneuvers on brain oxygenation and cerebral hemodynamics [42, 43, 48].

Automated Pupillometry

In the critical care setting, pupillary size and reactivity to light may provide information about intracranial disease, including elevated ICP and altered perfusion, sedation and analgesia, delirium assessment, brain metabolic derangements, and prognostication [49, 50]. Some studies have used pupillometry to assess the pupil-lary response to a light stimulus before painful procedures in order to assess adequacy of analgesia. In addition, pupillometry has been shown to be useful to assess the level of sedation, with a good correlation with BIS values [50].

Metabolic disorders can impair the sympathetic system and affect pupillary light reactivity. This can also be observed in patients with sepsis or liver-associated encephalopathy, and neurological disorders. Some authors have suggested that patients with a delayed recovery of pupillary reflexes developed demyelinating encephalopathy or dementia, suggesting that pupillary abnormalities may be associated with potential neurological derangements [49, 50].

Automated pupillometry is also gaining interest as part of the prognostication algorithms adopted after cardiac

arrest [49]. A pupillary light reflex < 6%, neurologic pupillary index (NPi) of 0 at 6 h from the cardiac arrest, and a pupillary light response < 13% have shown to be predictive of poor outcome [49]. Pupillary light reactivity, when used in combination with EEG and SSEP has also been shown to improve sensitivity to 100% for the prediction of outcome after cardiac arrest [49].

Intracranial hypertension can also occur in non-primary brain injured patients. Automated pupillometry can detect and even predict elevated ICP. For example, unilateral pupillary dilation and loss of reactivity can be detected as a sign of trans-tentorial herniation [49]. An altered constriction velocity has been identified during and before ICP elevation, and improvement in constriction velocity has been described after osmotic treatment to reduce brain edema [49].

At present, no consensus exists concerning the routine use of automated pupil-lometry in ED and ICU settings, although recent research supports its use to obtain objective information on pupillary function compared with manual pupillary examination [49, 50].

Conclusion

Increasing evidence suggests that the use of brain monitoring – EEG, evoked potentials, TCD, and NIRS – is gaining popularity even in non-neurocritical care settings, e.g., in the perioperative setting, ED, and ICU, to improve patient care. Neuromonitoring devices can be non-invasive, low-cost, safe tools available at the bedside, with a great potential for both diagnosis and monitoring of patients at risk of brain insult.

Further clinical and research developments, training and teaching programs are urgently needed to support implementation of neuromonitoring in daily clinical practice.

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None.

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References

1. Robba C, Goffi A, Geeraerts T, et al. Brain ultrasonography: methodology, basic and advanced principles and clinical applications. A narrative review. Intensive Care Med. 2019;45:913–27.
2. Bonatti G, Iannuzzi F, Amodio S, et al. Neuromonitoring during general anesthesia in non neurologic surgery. Best Pract Res Clin Anaesthesiol. 2021;35:255–66.
3. So VC, Poon CCM. Intraoperative neuromonitoring in major vascular surgery. Br J Anaesth. 2016;117:ii13-25.
4. Milne B, Gilbey T, Gautel L, Kunst G. Neuromonitoring and neurocognitive outcomes in cardiac surgery: a narrative review. J Cardiothorac Vasc Anesth. 2021. https://doi.org/10.1053/j.jvca.2021.07.029.
5. Checketts MR, Alladi R, Ferguson K, et al. Recommendations for standards of monitoring during anaesthesia and recovery 2015: Association of Anaesthetists of Great Britain and Ireland. Anaesthesia. 2016;71:85–93.
6. Romagnoli S, Franchi F, Ricci Z. Processed EEG monitoring for anesthesia and intensive care practice. Minerva Anestesiol. 2019;85:1219–30.
7. Aldecoa C, Bettelli G, Bilotta F, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. Eur J Anaesthesiol. 2017;34:192–214.
8. Roseborough GS. Pro: routine shunting is the optimal management of the patient undergoing carotid endarterectomy. J Cardiothorac Vasc Anesth. 2004;18:375–80.
9. Estruch-Pérez MJ, Barberá-Alacreu M, Ausina-Aguilar A, Soliveres-Ripoll J, Solaz-Roldán C, Morales-Suárez-Varela MM. Bispectral index variations in patients with neurological deficits during awake carotid endarterectomy. Eur J Anaesthesiol. 2010;27:359–63.
10. Wildes TS, Mickle AM, Ben Abdallah A, et al. Effect of electroencephalography-guided anesthetic administration on postoperative delirium among older adults undergoing major surgery. JAMA. 2019;321:473.
11. Sloan TB, Edmonds HL, Koht A. Intraoperative electrophysiologic monitoring in aortic sur3gery. J Cardiothorac Vasc Anesth. 2013;27:1364–73.
12. Cardim D, Robba C, Schmidt E, et al. Transcranial Doppler non-invasive assessment of intracranial pressure, autoregulation of cerebral blood flow and critical closing pressure during orthotopic liver transplant. Ultrasound Med Biol. 2019;45:1435–45.
13. Robba C, Bacigaluppi S, Cardim D, et al. Intraoperative non invasive intracranial pressure monitoring during pneumoperitoneum: a case report and a review of the published cases and case report series. J Clin Monit Comput. 2016;30:527–38.
14. Citerio G, Vascotto E, Villa F, Celotti S, Pesenti A. Induced abdominal compartment syndrome increases intracranial pressure in neurotrauma patients: a prospective study. Crit Care Med. 2001;29:1466–71.
15. Aguirre JA, Märzendorfer O, Brada M, Saporito A, Borgeat A, Bühler P. Cerebral oxygenation in the beach chair position for shoulder surgery in regional anesthesia: impact on cerebral blood flow and neurobehavioral outcome. J Clin Anesth. 2016;35:456–64.
16. Kietaibl C, Engel A, Horvat Menih I, et al. Detection and differentiation of cerebral microemboli in patients undergoing major orthopaedic surgery using transcranial Doppler ultrasound. Br J Anaesth. 2017;118:400–6.
17. Sloan MA. Prevention of ischemic neurologic injury with intraoperative monitoring of selected cardiovascular and cerebrovascular procedures: roles of electroencephalography, somatosensory evoked potentials,

transcranial doppler, and near-infrared spectroscopy. Neurol Clin. 2006;24:631–45.
18. Messerotti Benvenuti S, Zanatta P, Valfrè C, Polesel E, Palomba D. Preliminary evidence for reduced preoperative cerebral blood flow velocity as a risk factor for cognitive decline three months after cardiac surgery: an extension study. Perfusion. 2012;27:486–92.
19. Ono M, Joshi B, Brady K, et al. Risks for impaired cerebral autoregulation during cardiopulmonary bypass and postoperative stroke. Br J Anaesth. 2012;109:391–8.
20. Stilo F, Spinelli F, Martelli E, et al. The sensibility and specificity of cerebral oximetry, measured by INVOS - 4100, in patients undergoing carotid endarterectomy compared with awake testing. Minerva Anesth. 2012;78:1126–35.
21. Guay J, Kopp S. Cerebral monitors versus regional anesthesia to detect cerebral ischemia in patients undergoing carotid endarterectomy: a meta-analysis. Can J Anesth. 2013;60:266–79.
22. Thiele RH, Shaw AD, Bartels K, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on the role of Neuromonitoring in perioperative outcomes: cerebral near-infrared spectroscopy. Anesth Analg. 2020;131:1444–55.
23. Chan MJ, Chung T, Glassford NJ, Bellomo R. Near-infrared spectroscopy in adult cardiac surgery patients: a systematic review and meta-analysis. J Cardiothorac Vasc Anesth. 2017;31:1155–65.
24. de Azevedo DS, Salinet ASM, de Lima OM, Teixeira MJ, Bor-Seng-Shu E, de Carvalho NR. Cerebral hemodynamics in sepsis assessed by transcranial Doppler: a systematic review and meta-analysis. J Clin Monit Comput. 2017;31:1123–32.
25. Rasulo FA, Bertuetti R, Robba C, et al. The accuracy of transcranial Doppler in excluding intracranial hypertension following acute brain injury: a multicenter prospective pilot study. Crit Care. 2017;21:44.
26. Robba C, Pozzebon S, Moro B, Vincent J-L, Creteur J, Taccone FS. Multimodal non-invasive assessment of intracranial hypertension: an observational study. Crit Care. 2020;24:379.
27. Yigit O, Eray O, Mihci E, Yilmaz D, Arslan S, Eray B. The utility of EEG in the emergency department. Emerg Med J. 2012;29:301–5.
28. Fritz BA, Kalarickal PL, Maybrier HR, et al. Intraoperative electroencephalogram suppression predicts postoperative delirium. Anesth Analg. 2016;122:234–42.
29. Crepeau AZ, Rabinstein AA, Fugate JE, et al. Continuous EEG in therapeutic hypothermia after cardiac arrest: prognostic and clinical value. Neurology. 2013;80:339–44.
30. Choi WJ, Lee JH, Kim SH. Neurological prognostication using raw EEG patterns and spectrograms of frontal EEG in cardiac arrest patients. J Clin Neurophysiol. 2021. https://doi.org/10.1097/WNP.0000000000000787.
31. Koenig MA, Kaplan PW. Clinical applications for EPs in the ICU. J Clin Neurophysiol. 2015;32:472–80.
32. Peluso L, Rechichi S, Franchi F, et al. Electroencephalographic features in patients undergoing extracorporeal membrane oxygenation. Crit Care. 2020;24:629.
33. Cho S-M, Choi CW, Whitman G, et al. Neurophysiological findings and brain injury pattern in patients on ECMO. Clin EEG Neurosci. 2019;52:462–9.
34. Kubota T, Gajera PK, Kuroda N. Meta-analysis of EEG findings in patients with COVID-19. Epilepsy Behav. 2021;115:107682.
35. Ponziani FR, Funaro B, Lupascu A, et al. Minimal hepatic encephalopathy is associated with increased cerebral vascular resistance. A transcranial doppler ultrasound study. Sci Rep. 2019;9:15373.
36. Olguín-Ramírez L, Hernández-Guajardo D, Celis-Jasso J, et al. Difference of cerebral flows in uremia as a cause of encephalopathy. Follow-up by transcranial Doppler. Neurology. 2020;94:5413.
37. Mazeraud A, Righy C, Bouchereau E, Benghanem S, Bozza FA, Sharshar T. Septic-associated encephalopathy: a comprehensive review. Neurotherapeutics. 2020;17:392–403.
38. Szatmári S, Végh T, Csomós Á, et al. Impaired cerebrovascular reactivity in sepsis-associated encephalopathy studied by acetazolamide test. Crit Care. 2010;14:R50.
39. Pierrakos C, Attou R, Decorte L, et al. Transcranial Doppler to assess sepsis-associated encephalopathy in critically ill patients. BMC Anesthesiol. 2014;14:45.
40. Lemiale V, Huet O, Vigué B, et al. Changes in cerebral blood flow and oxygen extraction during post-resuscitation syndrome. Resuscitation. 2008;76:17–24.
41. Battaglini D, Santori G, Chandraptham K, et al. Neurological complications and noninvasive multimodal neuromonitoring in critically ill mechanically ventilated COVID-19 patients. Front Neurol. 2020;11:602114.
42. Robba C, Messina A, Battaglini D, et al. Early effects of passive leg-raising test, fluid chal lenge, and norepinephrine on cerebral autoregulation and oxygenation in COVID-19 critically ill patients. Front Neurol. 2021;12:674466.
43. Robba C, Ball L, Battaglini D, et al. Early effects of ventilatory rescue therapies on systemic and cerebral oxygenation in mechanically ventilated COVID-19 patients with acute respiratory distress syndrome: a prospective observational study. Crit Care. 2021;25:111.
44. Macdonald SPJ, Brown SGA. Near-infrared spectroscopy in the assessment of suspected sepsis in the emergency department. Emerg Med J. 2015;32:404–8.
45. Takegawa R, Hayashida K, Rolston DM, et al. Near-infrared spectroscopy assessments of regional cerebral oxygen saturation for the prediction of clinical outcomes in patients with cardiac arrest: a review of clinical impact, evolution, and future directions. Front Med. 2020;7:587930.
46. Macdonald SPJ, Kinnear FB, Arendts G, Ho KM, Fatovich DM. Near-infrared spectroscopy to predict organ failure and outcome in sepsis: the assessing risk in sepsis using a tissue oxygen saturation (ARISTOS) study. Eur J Emerg Med. 2019;26:174–9.
47. Donati A, Damiani E, Domizi R, Pierantozzi S, Calcinaro S, Pelaia P. Near-infrared spectroscopy to assess tissue oxygenation in patients with polytrauma: relationship with outcome. Crit Care. 2015;19:1308.
48. Khan I, Rehan M, Parikh G, et al. Regional cerebral oximetry as an indicator of acute brain injury in adults undergoing veno-arterial extracorporeal membrane oxygenation–a prospective pilot study. Front Neurol. 2018;9:993.
49. Bower MM, Sweidan AJ, Xu JC, Stern-Neze S, Yu W, Groysman LI. Quantitative pupillometry in the intensive care unit. J Intensive Care Med. 2021;36:383–91.
50. Phillips SS, Mueller CM, Nogueira RG, Khalifa YM. A systematic review assessing the current state of automated pupillometry in the neuroICU. Neurocrit Care. 2019;31:142–61.

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